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Characterization of genomic variations in SNPs of PE_PGRS genes reveals deletions and insertions in extensively drug resistant (XDR) *M. tuberculosis* strains from Pakistan

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ABSTRACT

Background: *Mycobacterium tuberculosis* (MTB) PE_PGRS genes belong to the PE multi-gene family. Although the function of the members of the PE_PGRS multi-gene family is not yet known, it is hypothesized that the PE_PGRS genes may be associated with genetic variability.

Material and methods: Whole genome sequencing analysis was performed on ($n = 37$) extensively drug resistant (XDR) MTB strains from Pakistan which included Central Asian ($n = 23$), East African Indian ($n = 2$), X3 ($n = 1$), T group ($n = 3$) and Orphan ($n = 8$) MTB strains. **Results:** By analyzing 42 PE_PGRS genes, 111 SNPs were identified, of which 13 were non-synonymous SNPs (nsSNPs). The nsSNPs identified in the PE_PGRS genes were as follows: 6, 9, 10 and 55 present in each of the CAS, EAI, Orphan, T1 and X3 XDR MTB strains studied. Deletions in PE_PGRS genes: 19, 21 and 23 were observed in 7 (35.0%) CAS1 and 3 (37.5%) in Orphan XDR MTB strains, while deletions in the PE_PGRS genes: 49 and 50 were observed in 36 (95.0%) CAS1 and all CAS, CAS2 and Orphan XDR MTB strains. An insertion in PE_PGRS6 gene was observed in all CAS, EAI3 and Orphan, while insertions in the PE_PGRS genes 19 and 33 were observed in 19 (95%) CAS1 and all CAS, CAS2, EAI3 and Orphan XDR MTB strains.

Conclusion: Genetic diversity in PE_PGRS genes contributes to antigenic variability and may result in increased immunogenicity of strains. This is the first study identifying variations in nsSNPs, Insertions and Deletions in the PE_PGRS genes of XDR-TB strains from Pakistan. It highlights common genetic variations which may contribute to persistence.

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